Journal of Food and Nutrition Research, 2022, Vol. 10, No. 10, 701-710 Available online at http://pubs.sciepub.com/jfnr/10/10/8 Published by Science and Education Publishing DOI:10.12691/jfnr-10-10-8



Potential Role of Cinnamon (Cinnamomum verum) to Reduce the Risk of Polycystic Ovary Syndrome by Managing the Obesity: A Review

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Received September 14, 2022; Revised October 17, 2022; Accepted October 28, 2022

Abstract The current study aims to assess the impact of obesity on polycystic ovary syndrome. It has a huge impact on the body, impacting physical, emotional, cognitive, and intellectual faculties. Diabetes mellitus, cardiovascular disease, endometrial cancer, and other clinical problems result. Insulin resistance, which refers to the process by which the body is unable to respond to insulin production sequentially, leading to a high level of triglycerides and cholesterol in the blood, is one of the most dangerous aspects studied in these individuals. Obesity is the leading cause of this condition, which is caused by an excessive buildup of fat in the body, which interferes with the body's natural functioning. Cardiovascular illnesses, which lead to a higher death rate globally, have a substantial relationship with PCOS. Women with PCOS have an increased amount of fatty tissues, which can worsen the condition and lead to type-II diabetes, stroke, and CVD. Physical manifestations of this heinous disease include acne, hirsutism, androgenetic alopecia, or male pattern baldness. Metabolic abnormalities contribute to the development and progression of PCOS and have major ramifications in later life that can be hazardous to health. It has been shown that even a 5% weight loss can reduce insulin and testosterone levels and improve fertility and menstrual cycle. Cinnamon has been shown to enhance menstrual cyclicity and insulin sensitivity in women with PCO. The purpose of this review is to investigate the efficacy of cinnamon supplementation in conjunction with specific lifestyle modifications, which has been proven to have potential therapeutic benefits against obesity and PCOS.

Keywords: hormonal issues, non-communicable diseases, Cinnamon

Cite This Article: Sana Noreen, Rabia Kanwal, Abdul Rehman, Ayesha Sadiqa, Fizza Mubarak, Madiha Khan Niazi, Ahasan Ullah Khan, and Yunita Sari Pane, "Potential Role of Cinnamon (*Cinnamomum verum*) to Reduce the Risk of Polycystic Ovary Syndrome by Managing the Obesity: A Review." *Journal of Food and Nutrition Research*, vol. 10, no. 10 (2022): 701-710. doi: 10.12691/jfnr-10-10-8.

1. Introduction

Polycystic ovarian syndrome is a problem that occurs as a result of hormonal imbalance and obesity, which is the primary cause of this disease. It is also known as Hyper androgenic Anovulation or Stein-Leventhal Syndrome since it was initially characterised as an oligoamenorrhea condition by Stein and Leventhal. It is a common metabolic disorder as well as a reproductive condition that affects females of reproductive age [1]. According to biochemical studies, people with this illness typically have

excessive cholesterol and triglycerides, which can lead to other metabolic problems. It is a syndrome in which one or both ovaries develop around 10 tiny cysts with diameters of 2mm and 9mm [2]. These cysts arise when the body attempts to ovulate but fails, resulting in tiny cysts. Overall, it affects 6-25% of females of reproductive age, although at the community level, its prevalence is lower in comparison to other disorders [3]. Non-insulindependent diabetes, high blood pressure, insulin resistance, and higher levels of all lipids or lipoproteins are examples of metabolic dysfunctions. Amenorrhea, which refers to the complete absence of menstruation, subfertility, and endometrial cancer, which develops in the uterus and

negatively affects other body processes as well as an elevated cell production rate, are reproductive difficulties similar to polycystic ovarian syndrome [4].

Women with PCOS may also experience depression, which causes relentless feelings of discomfort that affect the normal activity and the usefulness of bodily functions, lack of interest, abrupt mood fluctuations, unexplained weight gain, and issues with eating patterns of considerable interest [5]. It is also linked to cardiovascular illnesses, which are a group of ailments that lead to chest discomfort, artery blockage, and, ultimately, death. Intima medium thickness (IMT) in PCOS individuals causes the production of carotid artery plaque, which is connected with age, hypercholesterolemia, obesity, smoking, and diabetes, increasing the risk of stroke and heart attack in comparison to the same age group who do not have this disease [6]. It has also been discovered that total cholesterol, low-density lipoproteins, and triglycerides are greater, whereas highdensity lipoproteins are lower [7]. Many environmental and genetic variables contribute to the progression of this illness. The prevalence of common dermatologic symptoms in females suffering from acne (53%), hirsutism (65-70%), androgenic alopecia (33%), and seborrheic dermatitis (35%). It was first assumed that it was a condition that only affected adult women, but it has now been shown that it also occurs during the prenatal period. PCOS has a significant economic impact on several nations. Every year, over \$4 billion in the United States and \$800 million in Australia are spent on the treatment of problems caused by this ovarian condition [4]. Patients hospitalized to hospitals had double the proportion of those who have PCOS as those who do not. Using NIH standards, 10% of women of reproductive age are diagnosed with PCOS, however using Rotterdam criteria, more than 18% of females are affected. PCOS is seen in 80-90% of women who experience menstrual abnormalities [2].

Many research studies have recently been conducted to examine the effects of natural supplements and herbal therapy on PCOS and its associated issues. Cinnamon is a popular beneficial herbal ingredient all over the world, and its medicinal effects have been thoroughly researched [8]. Cinnamon has long been utilized as a traditional medicine in various parts of the world, including China, India, the Unitarian Church, and Iran. Cinnamon may be useful in the treatment of PCOS by boosting the activity of phosphatidylinositol 3-kinase in the insulin signaling pathway, hence improving insulin action. In accordance with this, growing data suggests that the presence of inositol is required for insulin sensitivity and activity, which might be considered beneficial. They influence insulin-stimulated glucose consumption in the cell via many mechanisms such as cellular absorption of glucose or glycogen formation; also, inositol improves multiple components of the metabolic syndrome such as glucose tolerance, blood pressure, and triglyceride levels. Furthermore, inositol may have a role in restoring fertility in PCOS women [9]. In oocytes and follicular cells, myo-inositol functions as a second messenger of the luteinizing hormone (LH) and follicle-stimulating hormone (FSH) signalling pathways. The amounts of myo-inositol in human follicular fluid regulate follicular maturity and oocyte quality. Cinnamon is a Cinnamomum bark that grows to be 5 to 7 meters tall and is constantly

Cinnamon contains numerous components (procyanidins, diterpenes, phenylpropanoids, mucilage, and polysaccharides), but cinnamaldehyde is the most significant. Cinnamon possesses anti-oxidant, antiinflammatory, anti-diabetic, anti-fungal, and anti-bacterial effects, as well as the ability to alleviate nausea and diarrhoea [10,11]. Many clinical investigations suggest that cinnamon supplementation has an influence and efficacy level on body mass index (BMI), hormonal imbalance, oxidative stress, fertility, and glucose homeostasis parameters in PCOS patients [12]. It has been used to treat a variety of illnesses, but additional study has lately been conducted to examine its impact on obesity, metabolic syndrome, and PCOS. The pathogenesis of polycystic ovarian syndrome, as well as its signs and symptoms, will be discussed in this review, as will the morbidities associated with the condition, the effect of cinnamon supplementation on PCOS, and the treatment necessary to control this problem.

2. Bioactive Components

Cinnamon's biological benefits are attributable to its bioactive component makeup. For the identification of these substances, liquid chromatography (LC) and gas chromatography (GC) are utilised, with the first being used to detect phenolic compounds and the second for volatiles analysis [13]. Table 1 lists the primary phenolic chemicals found in cinnamons.

Table 1.

| Compound | Unit (dry weight) | Cinnamon(dry weight) |
|---------------------------|----------------------|-------------------------|
| Rutin | mg/100g | 0.672 |
| Kaempferol | mg/100g | 0.016 |
| Quercetin | mg/100g | 0.172 |
| Catechin | mg/100g | 1.9 |
| Isorhamentin | mg/100g | 0.103 |
| Gallic acid | μg/g | 8.21 |
| p-Hydroxybenzoic acid | μg/g | 3.54 |
| Protocatechuic acid | μg/g | 281.2 |
| 3,4-Dihydroxybenzaldehyde | μg/g | 2.3 |
| p-Hydroxybenzaldehyde | μg/g | 0.4 |
| Salicylic acid | μg/g | 3.28 |
| Syringic acid | μg/g | 5.23 |
| Cinnamic acid | μg/g | 604.9 |
| p-Coumaric acid | μg/g | 1.81 |
| Vanillic acid | acid μg/g 0.89 | |
| Chlorogenic acid | μg/g | 9.46 |
| Vanillin | μg/g | 3.36 |
| Caffeic acid | μg/g | 0.81 |
| Catechin | mg/100g | 1057.7 |
| Caffeic acid | mg/100g | 15.3 |
| Cinnamyl aldehydes | mg/100g | 109.1 |

The effects of cinnamon on the cardiovascular system and the related biological activities (prediabetes, antiobesity, T2DM, antioxidant, PCOS, anti-inflammatory). It should be mentioned that most of the biological effects have been identified in extracts or supplements obtained from the bark of cinnamon as shown in Table 2.

Table 2. Protective activities of cinnamon in the cardiovascular system and other related effect

| Cinnamon Extract | Compounds | Study type | Results | Mechanism | References |
|--|---|--|--|--|------------|
| Aqueous, EtOH, MeOH | Fatty acids, phenolic acids, terpenes. | In vitro, In vivo, In silico. Inhibitory activity of α-amylase and α-glucosidase enzymes. In vivo: adult Albino Wistar male rats were STZ-induced diabetes | The extracts inhibit the enzymes, improve the diabetic state (normalize glucose, insulin, and other marker enzymes), and show a hypolipidemic effect | The effect is due to the synergistic effects of all the compounds present in ethanolic extract. The stimulating impact of the β-cells and the same drug also has the hypolipidemic effect | [14] |
| Standard Compounds | Cinnamic acid and (CD) cinnamic aldehyde (CA) | In vivo: 90 male Sprague- Dawley rats, were isoproterenol-induced acute myocardial ischemia. | Both compounds decreased the ST segment elevation induced by acute myocardial ischemia, decreased serum levels of CK-MB, LDH, TNF-α, and IL-6, increased serum NO activity, and SOD decreased MDA content in myocardial tissue. | The protection observed was attributable to antioxidant and anti-inflammatory properties, and increased NO. | [15] |
| Aqueous | Cinnamaldehyde, cinnamic acid, cinnamyl alcohol | In vitro: HDAC8 inhibitory effects | HDAC8 activity was significantly inhibited at 67 % | The phytochemicals act synergistically to induce the inhibition of the enzyme. | [16] |
| Spray-dried Aqueous extract | 4 % type A procyanidin polyphenols | clinical trial: Human studies (n = 137, W/M from China, mean age 61.3 ± 0.8 years, Fasting Serum Glucose (FSG): >6.1 mmol/L (HG), 56 % overweight CS, 14 % obese | Reduced fasting insulin, glucose, total and LDL cholesterol, enhanced insulin sensitivity. | Proanthocyanidins act as antioxidants by inhibiting the formation of AGEs and Increased GLUT4 | [17] |
| Extracts of DCM, EtOAc, EtOH, MeOH, and H2O | Phenolic acids, terpenes, and cinnamaldehyde | In vitro: Using RAW 264.7 and J7774A.1 macrophages. Determination of nitric oxide by the Griess assay. TNF-α by ELISA | anti-inflammatory activity inhibiting NO, TNF-α and LPS, IFN-γ in RAW 264.7 and J774A.1 macrophages. | Downregulated the proteins linked to inflammation | [18] |
| Aqueous | Trans- cinnamaldehyde, cinnamic acid, trans-cinnamic alcohol, eugenol, coumarin. | In vitro: rat aortic VSMC | Inhibited the platelet-derived growth factor PDGF-BB-induced VSMC proliferation and suppressed the PDGF-stimulated early signal transduction. Arrested the cell cycle and inhibited positive regulatory proteins. The protein levels of p21 and p27 increased, also the expression of proliferating cell nuclear antigen (PCNA) was inhibited by the cinnamon extract. Inhibited the VSMC Proliferation. | These effects were produced through a G0/G1 arrest, down-regulated the expression of cell cycle positive regulatory proteins by up-regulating p21 and p27 expression | [19] |
| Powder cinnamon bark mixed with a High-Fat/high- calorie meal | Polyphenols and<200 ppm Coumarin | Clinical trial: Human trial, n = 13 (7 M/6 W). 65 years old, BMI 28.0 kg m | Reduced glycemic response, postprandial endotoxemia, and C-reactive protein. Increased cholesterolemic response. | Modifying insulin or GLP-1 response | [20] |

3. Pathophysiology of Polycystic Ovary Syndrome

The pathogenesis of polycystic ovary syndrome is quite complicated. Obesity and ovarian dysfunction, which can lead to hormonal imbalances, are two hereditary and environmental variables that might contribute to the development of PCOS [21]. The release of luteinizing

hormone (LH) and follicle-stimulating hormone (FSH) aids in the correct functioning of the gonads, promoting the secretion of gonadal hormones such as testosterone, estrogen, and progesterone, and so regulates the reproductive process [22]. Hyper androgenemia is defined as elevated amounts of testosterone as well as elevated levels of androstenedione, which serves as an intermediary in the production of testosterone and dehydroepiandrosterone (DHEA) [21].

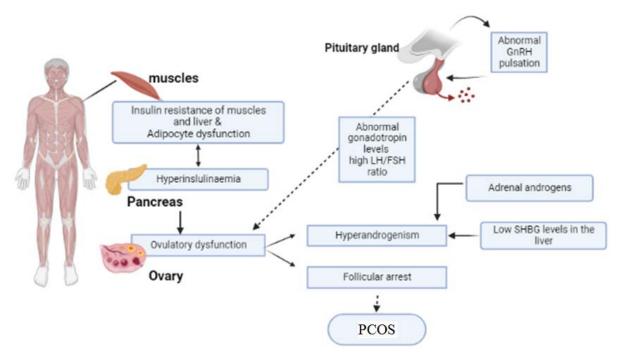


Figure 1. Correlations between anthropometry and lipid profile in women with PCOS

Women with PCOS have increased amounts of both androgen hormone and insulin. Many studies have shown that hyperinsulinemia is one of the key variables that contribute to the development of PCOS. Higher insulin levels stimulate the female ovary's release of the masculine hormone testosterone. It has been discovered that roughly 50-90% of females with PCOS have insulin resistance,

which leads to hyperinsulinemia. This insulin rise then collaborates with the luteinizing hormone. PCOS individuals have a mutation in LH G1052A, which affects the structure or function of LH and so contributes to the pathophysiology of this condition. A rise in luteinizing hormones raises testosterone levels as well as gonadotropin-releasing hormone, leading in an ovulation. [23].

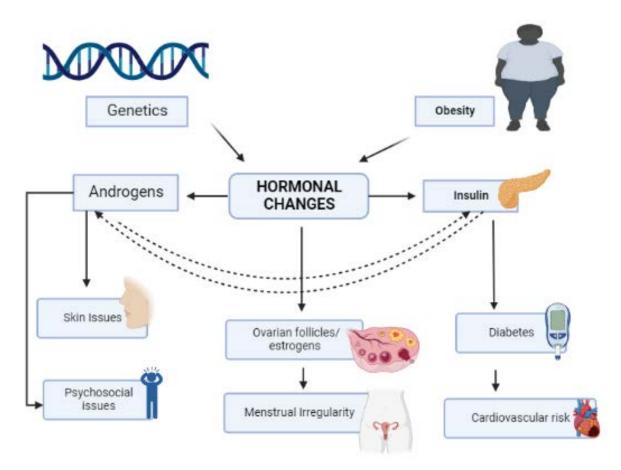


Figure 2. Androgens increase the accumulation of advanced glycation end products in granulosa cells by activating ER stress in PCOS

Insulin resistance influences the amount of sex hormone-binding globulin as well (SHBG). The most major androgenic hormone found in females is testosterone. Its levels in the body should be maintained. Testosterone may be present in both bound and free states. SHBG is important in binding sex hormones like testosterone and so controlling the level of free testosterone. Females with PCOS have low levels of this protein, therefore their testosterone levels are higher than in typical healthy females [24]. The granulosa cells of the follicles in the ovaries generate anti-Mullerian hormone (AMH). Polycystic ovarian syndrome develops as a result of an excess in this hormone [23]. Because the number of follicles in PCOS patients is large, it is hypothesized that the rise in AMH levels is related to an increase in the number of follicles engaged in AMH generation. AMH interferes with the actions of follicle-stimulating hormones [25]. Six hundred people with hirsutism were identified with PCOS in a study of 1000 patients with hyperandrogenism. Hirsutism is the occurrence of a male-like hair pattern on a female's face and body. It has been shown that 20 to 40% of girls with acne may have PCOS. Hair loss in women is extremely unpleasant, causing worry and sadness. PCOS is seen in 10% of women who have alopecia [12].

4. Associated Morbidities

4.1. Obesity and PCOS

The impact of PCOS on obesity is quite complicated. Obesity is more frequent in women with polycystic ovary syndrome than in women without the condition. PCOS affects 38-66% of overweight and obese women [26]. Females with PCOS have a bigger quantity of fat deposited in the upper half of their bodies. Being overweight affects PCOS signs and symptoms, while

being obese worsens the metabolic and reproductive features of PCOS [12]. Obesity is directly related to the development of PCOS. Obesity increases the amount of subcutaneous and visceral adipose tissues [27]. Obesity may contribute to the elevated level of cholesterol in this condition. Obesity, in addition to insulin resistance, causes quicker cortisol metabolism, which leads to hyperactivation of the hypothalamus-hypophysis adrenal axis (HHAA) and hence increases dehydroepiandrosterone (DHEA) synthesis [28]. Granular cell progesterone competes with cortisol, reducing cortisol's ability to bind to glucocorticoid receptors (GCR), which activate HHAA [29]. Obesity enhances aromatase expression, resulting in increased estrogen production in the ovaries. LH and FSH levels rise as a result of this. Chronic inflammation is caused by high amounts of leptin and leptin resistance, which alter the levels of LH releases and collagen in the ovaries [12]. Carbohydrate-rich diets can promote oxidative damage in blood cells, which can contribute to inflammation. Lipid-rich diets cause hyperandrogenemia by increasing testosterone production while decreasing SHBG protein synthesis. The intake of these diets has resulted in the accumulation of advanced glycation end products, which induce tissue damage to the ovaries [29].

An obese female with PCOS has a higher risk of acquiring metabolic syndromes, such as type 2 diabetes [30] and impaired glucose tolerance [30,31]. Obesity in these women also causes psychological problems such as worry or sadness. PCOS does not affect just obese women; it has also been observed in lean females. Obese women are more likely to get diseases such as breast cancer and endometrial cancer. Several studies have found that women with PCOS are more likely to acquire certain malignancies. The prevalence of polycystic ovarian syndrome in women is determined by their body mass index (BMI) in an unselected population of females looking for jobs in the health care field [32].

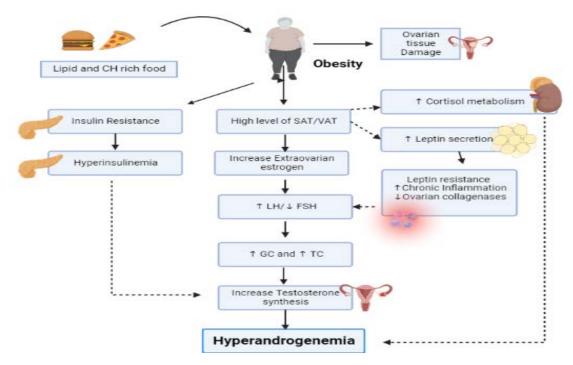


Figure 3. Navigating the pathophysiology of polycystic ovarian syndrome, insulin resistance, and obesity

4.2. Type 2 Diabetes

Multiple studies have identified a relationship between polycystic ovarian syndrome and non-insulin-dependent diabetes mellitus (type 2 diabetes), which might be attributed to the increased insulin resistance qualities reported in PCOS patients.

Type 2 diabetes develops earlier in women with PCOS than in women without PCOS. According to research, the incidence of type 2 diabetes in Italian ladies with PCOS is 2.6 times higher than in other females without the illness. This increase in the rate of acquiring type 2 diabetes is attributable to high BMI values and fasting glucose levels. In contrast, a high amount of sex-hormone-binding protein in plasma is associated with a lower risk of type 2 diabetes. Hyperandrogenism is also linked to an increased risk of type 2 diabetes. According to one study, the risk of T2DM in women with PCOS is four times higher than in healthy females. Females with PCOS who are young or middleaged have an increased chance of developing T2DM later in life, owing mostly to obesity and insulin resistance. One in every five women with PCOS will develop T2DM [2]. Insulin resistance is defined as the poor response of body cells to insulin, which results in a high amount of glucose in our bodies (insulin resistance in PCOS) PCOS development and progression are aided by metabolic abnormalities [33]. According to studies, 85% of PCOS patients have hyperinsulinemia, with 95% being obese and 65% being lean polycystic female patients. According to one study, lifestyle adjustments can improve insulin sensitivity by 70% in PCOS obese females for up to

6 months [2].

4.3. Cardiovascular Diseases

Cinnamaldehyde, cinnamic acid, eugenol, and coumarin are some of cinnamon's most significant chemicals. These compounds exhibit a wide range of biological actions, including antimicrobial, anti-inflammatory, antioxidant, antifungal, antidiabetic, and antiobesity properties [34]. Cinnamaldehyde is the primary bioactive molecule (60-75%), and it is widely used in the food sector due to its pleasant flavor [23]. This molecule is helpful and protective against cardiovascular illnesses such as cardiac ischemia, cardiac hypertrophy, and myocardial infarction [35,36] (Figure 4). Cinnamaldehyde (1-10 mg/kg) was shown to lower blood pressure in sedated dogs and guinea pigs in the early 1970s, which was attributed to its peripheral vasodilating actions. Hypotensive qualities were also seen in anaesthetized rats, which were explained by its negative inotropic and chronotropic effects on the heart, as well as its vasorelaxant action. They noticed that the vasodilatory activity cinnamaldehyde relaxed the rat aortic rings precontracted with phenylephrine, which was unaffected by the presence or absence of endothelium. Tarkhan et al. have demonstrated that this chemical protects against methylglyoxal-induced vascular injury in the rat thoracic aorta. Cinnamon chemicals include aromatic carboxylic acid, cinnamic acid, and other cinnamon compounds [37], also shown vasorelaxant actions in rat thoracic aortas [38] (Table 3).

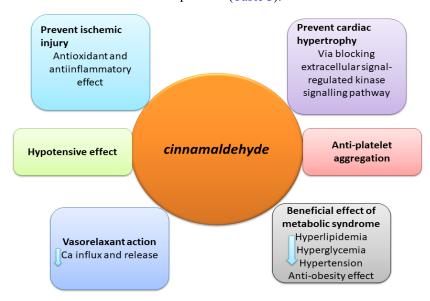


Figure 4. Cardiovascular effects of Cinnamaldehyde

Table 3. Effect of Bioactive components of cinnamon on CVD

| Bioactive component | Mechanism | References |
|---------------------|---|------------|
| | Vasorelaxant effects | [38] |
| Cinnamic acid | Protective effects against myocardial ischemia | |
| | Anti-obesity and cardioprotective | |
| Cinnamaldehyde | Delay the progression of cardiac hypertrophy and fibrosis | [39] |
| | Protect endothelial dysfunction under high glucose conditions | |
| | Vasculoprotective effects in Hypercholesterolemic rabbits | [40] |
| | Vasculoprotective effects | |
| | Prevent the development of atherosclerotic lesions | [41] |
| | Cytoprotective and anti inflammatory effect | [37,35] |

Lipid dysfunction in PCOS individuals raises the risk of cardiovascular disease. Females with PCOS had higher triglyceride levels of 26.39mg/dl, higher non-HDL cholesterol levels of 18.82mg/dl, and lower high-density lipoprotein concentrations of 6.41mg/dl, which raises the risk of developing cardiovascular disorders. Women with PCOS have an increased amount of fatty tissues, which can worsen the condition and lead to type 2 diabetes, stroke, and CVD. PCOS patients contribute to the development of endometrial cancer through factors such as obesity, type 2 diabetes, and anovulation, which raises estrogen levels in the body, leading in the production of such cancer. Several studies have found that obese females with PCOS are at a higher risk of acquiring cancer [2].

5. Treatment of Polycystic Ovary Syndrome with Cinnamon

Endocrinologists, pediatricians, gynecologists, dermatologists, and psychologists are commonly used to treat PCOS symptoms such as hirsutism and acne [2]. The American task committee and the Australian Alliance Guidelines provide treatment guidelines for PCOS.

5.1. Cinnamon Supplementation and PCOS

Because of the side effects - effects caused by medical therapies, there has recently been a shift in emphasis toward natural supplements and herbal medicine. Natural products give several health benefits while posing little or no risks. Cinnamon has long been used in traditional medicine to treat a number of disorders such as

amenorrhea, frigidity, headache, fever, common cold, diarrhea, toothache, flatulence, and so on [33]. Over the last decade, several research has been undertaken to study the effects of cinnamon supplementation on obesity, BMI, diabetes, metabolic syndrome, oxidative stress-related health problems, and PCOS [42].

Cinnamon has been studied for its effects on the cardiovascular system, primarily for its cardiovascular preventive characteristics. Furthermore, comorbidities such as diabetes and other metabolic illnesses enhance the likelihood of cardiovascular pathologies. Insulin resistance causes free radical production, which contributes to hypertension and endothelial dysfunction. Low insulin sensitivity is also linked to another metabolic syndrome (MetS) variables such as visceral obesity, hypertension, dyslipidemia, elevated proinflammatory cytokines, microalbuminuria, increased low-density lipoproteins, and reduced high-density lipoproteins [43,44,45]. The most often documented anti-obesogenic bioactive components in cinnamon are eugenol, cinnamaldehyde, and cinnamic acid, which improve glucose absorption and insulin sensitivity. However, in vitro models in 3T3-L1 adipocytes show that the reported effects are related to an increase in IR, GLUT4 and TTP, mRNA levels for GLUT1, GLUT4 translocation, phosphorylation of AMPK and ACC, lipid storage accumulation and fatty acid oxidation, mRNA levels for CPT1, PGC1, PPAR, and CIDEA, expression of PLIN and GPDH, and decreased levels of CPT1α, PGC1α, PPARγ, and CIDEA, expression of PLIN and GPDH, and reduced the levels of mRNA levels for GSK3β, IGF1R, IGF2R, PIK3R1, adiponectin secretion, expression of PLIN and GPDH, C/EBPα, and PPARγ [46].

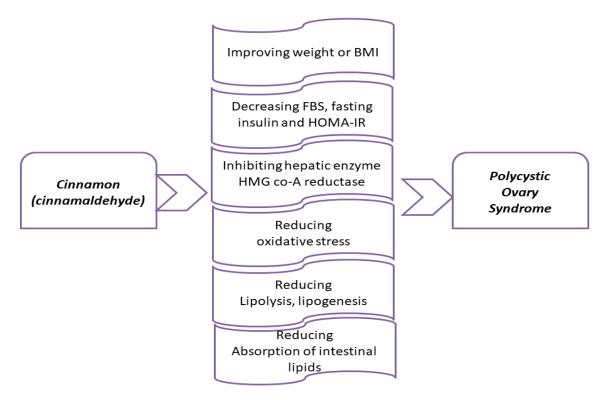


Figure 5. Cinnamon supplementation and PCOS

5.2. Cinnamon Supplementation

When compared to placebo, cinnamon supplementation resulted in a significant decrease in weight, BMI, serum fasting blood glucose levels, insulin levels, levels of lowdensity lipoproteins, serum triglycerides, and total cholesterol, as well as a significant increase in levels of high-density lipoproteins [8]. Cinnamon has also been shown in Figure 5 to have an insulin-sensitizing effect, which is linked to improved menstrual cyclicity in PCOS patients. A study found that cinnamon supplementation restored menstrual cyclicity and ovarian morphology in a DHEAinduced PCOS mouse model. Furthermore, the cinnamontreated group showed a substantial drop in serum levels of total testosterone, insulin, IGF-1, and LH, as well as a rise in serum FSH levels. Cinnamon powder capsules were reported to lower levels of low-density lipoproteins, fasting insulin, and insulin homeostatic model evaluation in PCOS women. Cinnamon supplementation increased antioxidant status and serum lipid profile in PCOS patients and may be useful in lowering PCOS risk factors and consequences [8]. A study was done to see how cinnamon supplementation affected metabolic dysfunction and menstrual cyclicity in PCOS patients. According to the findings, cinnamon supplementation improves menstrual cyclicity and can be utilized as an effective therapy option for patients with Polycystic Ovarian Syndrome. As a result, the research findings listed above imply that cinnamon can be utilized as an effective treatment agent for PCOS [42].

5.3. Lifestyle Modifications

Because obesity is a major contributor to the development of PCOS, it is suggested that you exercise and eat a well-balanced diet to keep your weight in check. As a result, lifestyle adjustments are critical in the treatment of PCOS. It has been discovered that even a 5% weight loss can reduce insulin and testosterone levels, improving fertility and the menstrual cycle [2]. Other lifestyle variables, like alcohol intake, psychological stresses, and smoking, must also be modified in the longterm therapy of PCOS. Exercise is an excellent supplement to any way of life. It is beneficial to the mind, body, and soul [47]. It appears to restore ovulation in obese women with PCOS, in addition to burning fat and decreasing the risk of heart disease and type 2 diabetes. It was also shown that consistent and non-dramatic weight loss as a consequence of exercise and good lifestyle modifications resulted in a decrease of central fat and enhanced insulin sensitivity, restoring ovulation in overweight infertile women with PCOS. Obese women who want to enhance their reproductive function should start with lifestyle changes.

6. Conclusion

The prevalence of PCOS is expected to rise as the obesity pandemic expands and the world population grows. Given our hereditary tendency for weight gain and the development of PCOS in certain women. Obesity is common in PCOS and aggravates many of the condition's

reproductive and metabolic symptoms. The relationship between PCOS and obesity is complex. Lifestyle and nutritional changes are essential to control PCOS and obesity. Cinnamon also has an influences estrous cyclicity and ovary shape, reduces blood testosterone and insulin levels, and lowers IGF-1 levels in plasma while increasing IGFBP-1 levels. Cinnamon has been proposed as a potential treatment for PCOS.

Abbreviations

PCOS: **Polycystic** Syndrome; Ovary cardiovascular disease; T2DM: Type II diabetes, IMT: Intima media thickness; LDL: low-density lipoproteins; HDL: high-density lipoproteins; BMI: body mass index; LH: luteinizing hormone; FSH: folliclestimulating hormone; DHEA: dehydroepiandrosterone; SHBG: sex hormone-binding globulin; AMH: Anti-Mullerian Hormone; HHAA: hypothalamus- hypophysis adrenal axis; GC: granular cells; GCR: glucocorticoid receptors; AGE: Advanced glycation end products; IGF-1: Insulin-like Growth Factor 1; IGFBP-1: Insulin-like Growth Factor Binding Protein-1

Author Contributions

This work was conducted in collaboration with all authors. Author SN and AUK planned, and structured the manuscript. SN wrote, revised, and rechecked the manuscript thoroughly. AUK, ST, and YSP improved the draft copy. RR, MU, and YSP contributed to revise and improve the manuscript thoroughly. All authors reviewed carefully and approved the final version of the manuscript.

Conflict of Interest

Authors declare that there is no conflict of interest

Funding Agency

The study was not funded by any authority

Availability of Data and Materials

All data generated and analyzed during this study are included in this article.

Ethics Approval and Consent to Participate

Not applicable.

Consent for Publication

Not applicable.

References

- [1] Hart R, Doherty DA. The potential implications of a PCOS diagnosis on a woman's long-term health using data linkage. The journal of clinical endocrinology & metabolism. 2015 Mar 1; 100(3): 911-9.
- [2] El Hayek S, Bitar L, Hamdar LH, Mirza FG, Daoud G. Poly cystic ovarian syndrome: an updated overview. Frontiers in physiology. 2016 Apr 5; 7: 124.
- [3] Palomba S, Falbo A, Daolio J, Battaglia FA, La Sala GB. Pregnancy complications in infertile patients with polycystic ovary syndrome: updated evidence. Minerva Ginecologica. 2018 Apr 11; 70(6): 754-60.
- [4] Chen ZJ, Shi Y, Sun Y, Zhang B, Liang X, Cao Y, Yang J, Liu J, Wei D, Weng N, Tian L. Fresh versus frozen embryos for infertility in the polycystic ovary syndrome. N engl j med. 2016 Aug 11; 375: 523-33.
- [5] Bagudu KA, Noreen S, Rizwan B, Bashir S, Khan M, Chishti K, Hussain S, Wahid S. Intermittent fasting effect on weight loss: a systematic review. Biosci Res. 2021; 18: 622-31.
- [6] Noreen S, Rizwan B, Khan M, Farooq S. Health benefits of Buckwheat (Fagopyrum esculentum), potential remedy for diseases, rare to cancer: A mini Review. Infectious Disorders-Drug Targets (Formerly Current Drug Targets-Infectious Disorders). 2021 Sep 1; 21(6): 15-20.
- [7] Malik S, Sheikh ZI, Kausar S, Ahmed N. Comparison of efficacy of spironolactone plus oral contraceptives with metformin in patients of PCOS with hirsutism. PAFMJ. 2018 Oct 30; 68(3): 460-65.
- [8] Borzoei A, Rafraf M, Niromanesh S, Farzadi L, Narimani F, Doostan F. Effects of cinnamon supplementation on antioxidant status and serum lipids in women with polycystic ovary syndrome. Journal of traditional and complementary medicine. 2018 Jan 1; 8(1): 128-33.
- [9] Laganà AS, Garzon S, Casarin J, Franchi M, Ghezzi F. Inositol in polycystic ovary syndrome: restoring fertility through a pathophysiology-based approach. Trends in endocrinology & metabolism. 2018 Nov 1; 29(11): 768-80.
- [10] Kumar S, Kumari R. Cinnamomum: review article of essential oil compounds, ethnobotany, antifungal and antibacterial effects. Open Access J Sci. 2019; 3(1): 13-6.
- [11] Dou L, Zheng Y, Li L, Gui X, Chen Y, Yu M, Guo Y. The effect of cinnamon on polycystic ovary syndrome in a mouse model. Reproductive Biology and Endocrinology. 2018 Dec; 16(1): 1-0.
- [12] Rodgers RJ, Avery JC, Moore VM, Davies MJ, Azziz R, Stener-Victorin E, Moran LJ, Robertson SA, Stepto NK, Norman RJ, Teede HJ. Complex diseases and co-morbidities: polycystic ovary syndrome and type 2 diabetes mellitus. Endocrine Connections. 2019 Mar 1: 8(3): R71-5.
- [13] Andrade M, Ribeiro-Santos R, Melo N, Sanches-Silva A. Bioactive compounds of cinnamon: a valuable aromatic plant for food packaging. InInternational Conference on Safety and Innovation in Food Packaging (InSIPack), 16 junho 2016 2016.
- [14] Vijayakumar K, Prasanna B, Rengarajan RL, Rathinam A, Velayuthaprabhu S, Vijaya Anand A. Anti-diabetic and hypolipidemic effects of Cinnamon cassia bark extracts: an in vitro, in vivo, and in silico approach. Archives of Physiology and Biochemistry. 2020 Sep 25: 1-1.
- [15] Sun P, Li K, Wang T, Ji J, Wang Y, Chen KX, Jia Q, Li YM, Wang HY. Procyanidin C1, a component of cinnamon extracts, is a potential insulin sensitizer that targets adipocytes. Journal of Agricultural and Food chemistry. 2019 Jul 23; 67(32): 8839-46.
- [16] Patil M, Choudhari AS, Pandita S, Islam MA, Raina P, Kaul-Ghanekar R. Cinnamaldehyde, cinnamic acid, and cinnamyl alcohol, the bioactives of Cinnamomum cassia exhibit HDAC8 inhibitory activity: an in vitro and in silico study. Pharmacognosy Magazine. 2017 Oct; 13(Suppl 3): S645.
- [17] Anderson RA, Zhan Z, Luo R, Guo X, Guo Q, Zhou J, Kong J, Davis PA, Stoecker BJ. Cinnamon extract lowers glucose, insulin and cholesterol in people with elevated serum glucose. Journal of traditional and complementary medicine. 2016 Oct 1; 6(4): 332-6.
- [18] Gunawardena D, Karunaweera N, Lee S, van Der Kooy F, Harman DG, Raju R, Bennett L, Gyengesi E, Sucher NJ, Münch G. Anti-inflammatory activity of cinnamon (C. zeylanicum and C. cassia) extracts-identification of E-cinnamaldehyde and

- o-methoxy cinnamaldehyde as the most potent bioactive compounds. Food & function. 2015; 6(3): 910-9.
- [19] Kwon H, Lee JJ, Lee JH, Cho WK, Gu MJ, Lee KJ, Ma JY. Cinnamon and its components suppress vascular smooth muscle cell proliferation by up-regulating cyclin-dependent kinase inhibitors. The American Journal of Chinese Medicine. 2015 Jun 29; 43(04): 621-36.
- [20] Furlan CP, Valle SC, Maróstica Jr MR, Östman E, Björck I, Tovar J. Effect of bilberries, lingonberries and cinnamon on cardiometabolic risk-associated markers following a hypercalorichyperlipidic breakfast. Journal of functional foods. 2019 Sep 1; 60: 103443
- [21] Ibáñez L, Oberfield SE, Witchel S, Auchus RJ, Chang RJ, Codner E, Dabadghao P, Darendeliler F, Elbarbary NS, Gambineri A, Rudaz CG. An international consortium update: pathophysiology, diagnosis, and treatment of polycystic ovarian syndrome in adolescence. Hormone research in paediatrics. 2017; 88: 371-95.
- [22] Fernandez RC, Moore VM, Van Ryswyk EM, Varcoe TJ, Rodgers RJ, March WA, Moran LJ, Avery JC, McEvoy RD, Davies MJ. Sleep disturbances in women with polycystic ovary syndrome: prevalence, pathophysiology, impact and management strategies. Nature and science of sleep. 2018; 10: 45.
- [23] Zou J, Wu D, Liu Y, Tan S. Association of luteinizing hormone/choriogonadotropin receptor gene polymorphisms with polycystic ovary syndrome risk: a meta-analysis. Gynecological Endocrinology. 2019 Jan 2; 35(1): 81-5.
- [24] Thathapudi S, Kodati V, Erukkambattu J, Addepally U, Qurratulain H. Association of luteinizing hormone chorionic gonadotropin receptor gene polymorphism (rs2293275) with polycystic ovarian syndrome. Genetic testing and molecular biomarkers. 2015 Mar 1; 19(3): 128-32.
- [25] Owens LA, Kristensen SG, Lerner A, Christopoulos G, Lavery S, Hanyaloglu AC, Hardy K, Yding Andersen C, Franks S. Gene expression in granulosa cells from small antral follicles from women with or without polycystic ovaries. The Journal of Clinical Endocrinology & Metabolism. 2019 Dec; 104(12): 6182-92.
- [26] Tufail T, Ijaz A, Noreen S, Arshad MU, Gilani SA, Bashir S, Din A, Shahid MZ, Khan AA, Khalil AA, Awuchi CG. Pathophysiology of Obesity and Diabetes. InDietary Phytochemicals 2021 (pp. 29-42). Springer, Cham.
- [27] Gebara N, Kim JY, Tapanainen J, Morin-Papunen L, Arslanian S. OR33-1 Metabolic Inflexibility in Obese versus Lean Women with Polycystic Ovary Syndrome (PCOS): Is PCOS Status or Adiposity the Critical Factor?. Journal of the Endocrine Society. 2019 Apr;3(Supplement_1): OR33-1.
- [28] Barber TM, Joharatnam J, Franks S. Pathogenesis and management of adiposity and insulin resistance in polycystic ovary syndrome (PCOS). InPediatric Obesity 2018 (pp. 629-642). Humana Press, Cham.
- [29] Greenwood E, Sroga-Rios J, Pavone M, Cedars M, Legro RS, Huddleston HG. Putative role for adiposity reducing antimullerian hormone production in polycystic ovary syndrome and community controls. Fertility and Sterility. 2018 Sep 1; 110(4): e123-4.
- [30] Mubarak SM, Ali HA. Phenotypes and Complications of Polycystic Ovary Syndrome: A Rapid Update: a review. Annals of Tropical Medicine and Public Health. 2020 Jun; 23: 23-1040.
- [31] Forslund M, Landin-Wilhelmsen K, Krantz E, Trimpou P, Schmidt J, Brännström M, Dahlgren E. No difference in quality of life or depression/anxiety diagnosis between middle-aged women with PCOS and age-matched controls. Maturitas. 2019 Jun 1; 124: 154.
- [32] Shandley LM, Fothergill A, Spencer JB, Mertens AC, Cottrell HN, Howards PP. Impact of cancer treatment on risk of infertility and diminished ovarian reserve in women with polycystic ovary syndrome. Fertility and sterility. 2018 Mar 1; 109(3): 516-25.
- [33] Adeghate E, Mohsin S, Adi F, Ahmed F, Yahya A, Kalász H, Tekes K, Adeghate EA. An update of SGLT1 and SGLT2 inhibitors in early phase diabetes-type 2 clinical trials. Expert opinion on investigational drugs. 2019 Sep 2; 28(9): 811-20.
- [34] Mousavi SM, Jalilpiran Y, Karimi E, Aune D, Larijani B, Mozaffarian D, Willett WC, Esmaillzadeh A. Dietary intake of linoleic acid, its concentrations, and the risk of type 2 diabetes: a systematic review and dose-response meta-analysis of prospective cohort studies. Diabetes Care. 2021 Sep 1; 44(9): 2173-81.
- [35] Moraes FD, Dubois Filho DG, Caliari ÁI, Brasil GA, do Nascimento AM, Kalil IC, Scherer R, Endringer DC, Lenz D, de

- Lima EM, de Andrade TU. Chronic treatment with cinnamaldehyde prevents spontaneous atherosclerotic plaque development in ovariectomized LDLr-/-female mice. Pharma Nutrition. 2020 Sep 1; 13: 100205.
- [36] Husain I, Ahmad R, Chandra A, Raza ST, Shukla Y, Mahdi F. Phytochemical characterization and biological activity evaluation of ethanolic extract of Cinnamomum zeylanicum. Journal of ethnopharmacology. 2018 Jun 12; 219: 110-6.
- [37] Tarkhan MM, Balamsh KS, El-Bassossy HM. Cinnamaldehyde protects from methylglyoxal-induced vascular damage: Effect on nitric oxide and advanced glycation end products. Journal of food biochemistry. 2019 Jul; 43(7): e12907.
- [38] Kang YH, Kang JS, Shin HM. Vasodilatory effects of cinnamic acid via the nitric oxide-cGMP-PKG Pathway in rat thoracic aorta. Phytotherapy Research. 2013 Feb; 27(2): 205-11.
- [39] Yang L, Wu QQ, Liu Y, Hu ZF, Bian ZY, Tang QZ. Cinnamaldehyde attenuates pressure overload-induced cardiac hypertrophy. International journal of clinical and experimental pathology. 2015; 8(11): 14345.
- [40] Wang F, Pu C, Zhou P, Wang P, Liang D, Wang Q, Hu Y, Li B, Hao X. Cinnamaldehyde prevents endothelial dysfunction induced by high glucose by activating Nrf2. Cellular Physiology and Biochemistry. 2015; 36(1): 315-24.
- [41] Nour OA, Shehatou GS, Rahim MA, El-Awady MS, Suddek GM. Cinnamaldehyde exerts vasculoprotective effects in

- hypercholestrolemic rabbits. Naunyn-Schmiedeberg's Archives of Pharmacology. 2018 Nov; 391(11): 1203-19.
- [42] Heydarpour F, Hemati N, Hadi A, Moradi S, Mohammadi E, Farzaei MH. Effects of cinnamon on controlling metabolic parameters of polycystic ovary syndrome: A systematic review and meta-analysis. Journal of ethnopharmacology. 2020 May 23; 254: 112741.
- [43] Khan AU, Khan AU, Khanal S, Subodh Gyawali. Insect pests and diseases of cinnamon (Cinnamomum verum Presi.) and their management in agroforestry system: A review. Acta Entomology and Zoology 2020; 1(2): 51-59.
- [44] Mollazadeh H, Hosseinzadeh H. Cinnamon effects on metabolic syndrome: a review based on its mechanisms. Iranian journal of basic medical sciences. 2016 Dec; 19(12): 1258.
- [45] Pulungan A and Pane YS. The benefit of cinnamon (*Cinnamonum burmannii*) in lowering total cholesterol levels after consumption of high-fat containing foods in white mice (*Mus musculus*) models [version 2; peer review:2 approved]. *F1000Research*. 2020, 9: 168.
- [46] Lu M, Cao Y, Xiao J, Song M, Ho CT. Molecular mechanisms of the anti-obesity effect of bioactive ingredients in common spices: a review. Food & function. 2018; 9(9): 4569-81.
- [47] Nawaz HH, Farooq S, Rizwan B, Noreen S, Azhar S, Bukht H, Fatima A, Ashraf A, Abid F. Junk and Fast Food Consumption among Obese University Students.



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